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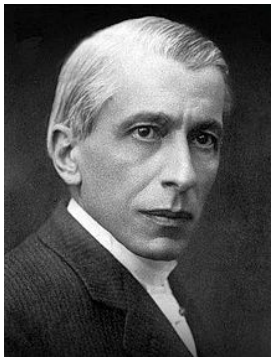
A Neglected Giant of Medical Science

Review of *The Priority of N. C. Paulescu in the Discovery of Insulin*, by Ion Pavel (Bucharest: Academy of the Socialist Republic of Romania, 1976), 251 pages

Reviewed by Mark Weber

No award is more highly regarded around the world than the Nobel Prize. It is the most coveted recognition of exceptional achievement in the major fields of human endeavor. Despite its prestige, the Prize is not an infallible indication of merit. Literary giants such as Leo Tolstoi, Theodore Dreiser and Anton Chekhov were passed over in favor of unquestionably less-deserving writers. The Peace Prize award to Henry Kissinger (with Le Duc Tho) in 1973 and to Menachem Begin (with Anwar Sadat) in 1978 provoked intense worldwide controversy.



N. C. Paulescu

In 1923, the Nobel Prize for Medicine was awarded jointly to Sir Frederick G. Banting, a Canadian, and John J. R. Macleod, a Scotsman, for the discovery of insulin, one of the greatest medical advances of modern times.

Insulin is a hormone produced by cells in the pancreas that regulate sugar production in the human body. The discovery of insulin has saved countless victims of diabetes from death, allowing them to lead practically normal lives. Largely because of the 1923 Nobel award, standard reference works credit Banting and his Toronto co-workers, Macleod and Charles H. Best, with this epochal medical breakthrough.

However, a substantial body of persuasive evidence indicates that the Nobel Committee made a major error in 1923, and that the award should rightfully have gone to an almost forgotten Romanian physiologist, Nicolae Paulescu. The only book available in English that makes the case for Paulescu is this passionately argued but poorly organized volume published in 1976. The work was put together by Ion Pavel, an elderly Bucharest scholar who has championed Paulescu's case for years in various journals and at international scientific conferences. Unfortunately, Pavel's often cumbersome and opaque writing style, poor translations, and the book's confusing organization are unworthy of Paulescu and his pioneering work. In spite of this, it is a valuable contribution to the history of twentieth century science.

Nicolae Constantin Paulescu was born in Bucharest in 1869. He received his medical education in Paris, where his extraordinary devotion and skills as a researcher won him special acclaim. During his stay in France, he proved himself a careful and critical observer.

In 1900 Paulescu returned to his beloved Romanian homeland, and during the next decade became internationally recognized as an experimental physiologist of exceptional ability. For 30 years he conducted extensive research at the University of Bucharest. During his lifetime he contributed nearly 90 scholarly papers to numerous European scientific journals. In 1903 he began publication of the monumental four-volume *Traité de Médecine*, which he wrote with the late Paris professor Dr. Etienne Lancereaux. Paulescu authored the massive three-volume *Traité de Physiologie Médicale* (2110 pages), published in 1919-1921.

Nicolae Paulescu was not merely an outstanding scientist. He was a remarkably decent man whose generosity and patience earned him the love of his devoted students. And he was an ardent patriot who loved his nation with characteristic Romanian fervor.

Paulescu's most important achievement was his successful isolation of the pancreas hormone that regulates the blood sugar level. He began work in this field in 1916, but the First World War interrupted his investigation. In 1921 he announced the discovery of the hormone extract, which he called "pancreine," now known universally as insulin.

Naturally, Paulescu was shocked by the Nobel Committee's 1923 decision. He protested, but without success. As a matter of policy, the Committee refuses to reconsider awards once made. Shortly before his death from cancer in 1931, Paulescu recorded his bitter disappointment in these lines:

"Formerly I believed and maintained that a scientist can work in perfect safety, convinced as I was that the date of his publications protected him – against any injustice. Unfortunately, I am obliged to admit now that I was utterly mistaken in this regard.

"I am not dominated by pride and I struggle against this odious vice. Indeed, on publishing my discovery I never for one moment thought of publicity, which could have affected my modesty that I consider one of the first qualities of a scientist. But I certainly cannot accept another, more odious defect, that of the theft of someone else's scientific property."

Paulescu's passing was an occasion of national mourning. Romanians turned out in great numbers to pay their last respects to a brilliant and devoted son who had brought great honor to his nation.

Paulescu announced his discovery of "pancreine" (insulin) in several scientific papers published between April and August 1921. The most comprehensive of these, and the one that best documented his claim as the pioneer discoverer of insulin, was received for publication by the widely respected *Archives Internationales de Physiologie* of Liège and Paris on June 22, 1921, and appeared in the issue of August 31, 1921. In it, Paulescu recorded his success in isolating the antidiabetic hormone of the pancreas and in using it to lower the blood sugar levels in both diabetic and normal dogs. The paper by Banting and Best that announced their own "discovery" of insulin was first read on December 31, 1921 and appeared in the February 1922 issue of the Toronto *Journal of Laboratory and Clinical Medicine*.

Just about the only thing the two papers have in common is their announcement of the same “discovery” of an antidiabetic hormone extract. The Paulescu article not only appeared five months earlier than the Canadian paper, but was significantly more comprehensive and scholarly. That is not at all surprising in light of the well-documented immaturity and inexperience of Banting and Best.

If Paulescu was the real discoverer of insulin, how was it that the Nobel Committee decided to credit Banting and Macleod with the achievement? A major reason was the fact that although Paulescu was the first to successfully isolate insulin and use it to treat diabetes in dogs, Banting, Best, and Macleod were the first to use it on humans. Furthermore, an associate of theirs, J.B. Collip, prepared a purer insulin from the extract and began producing it on a large scale, thus making it available to the public. Not surprisingly, the North American and European press enthusiastically hailed the Toronto team as the discoverers of insulin.

Another important factor was the Nobel Committee’s acceptance of an inexcusably erroneous description of Paulescu's work by Banting and Best in their paper published in February 1922. Their article mentions Paulescu’s earlier research, but falsely reports that the Romanian physiologist's injections of pancreas hormone extract into dogs had produced no effects. The crucial, oddly-worded passage read: “He [Paulescu] states that injections into peripheral veins produce no effect and his experiments show that second injections do not produce such marked effect as the first.” In reaching its decision on the award for the discovery of insulin, the Nobel Committee obviously failed to critically compare the claims of Banting, Best and Macleod against Paulescu’s papers.

Years later, Charles Best apologized for the crucial misrepresentation. “I regret very much that there was an error in our translation of Professor Paulescu’s article,” he wrote in a letter of October 15, 1969 to Ion Pavel. “I cannot recollect, after this length of time, exactly what happened ... I do not remember whether we relied on our own poor French or whether we had a translation made. In any case I would like to state how sorry I am for this unfortunate error and I trust that your efforts to honor Professor Paulescu will be rewarded with great success.”

Rolf Luft, president of the International Diabetes Foundation and chairman of the Nobel Committee for Physiology and Medicine, wrote in a 1971 article, “Who Discovered Insulin?”: “One fact remains, namely that the earlier discovery made by Paulescu was misinterpreted by Banting and Best for reasons which we cannot know anything about today ... In my opinion, the [Nobel] prize should – without any doubt – have been shared between Paulescu, Banting and Best ...” Prof. Eric Martin of Geneva noted in 1971 in a Swiss medical journal: “Thus, probably due to their poor knowledge of French, the merit of the Romanian scholar is reduced to naught.”

Actually, there are grounds for believing that the misrepresentation by Banting and Best was not merely a case of negligent translation, but was deliberate.

Several prominent scholars have condemned the Nobel Committee's injustice against Paulescu. Nobel Institute Director and 1948 Nobel Chemistry Prize winner, Prof. Arne Tiselius, stated in a December 1969 letter: “In my opinion, Paulescu was equally worthy of the award ... Unfortunately, there is no mechanism whereby the Nobel Committee could do anything now in this or similar cases. Personally, I can only hope that in an eventual celebration of the 50th anniversary of the discovery of insulin, due regard is paid to the pioneer work of Paulescu.”

Prof. Ian Murray, an internationally regarded physiologist, was particularly active in working to correct the historical wrong against Paulescu. Murray was eminently qualified to speak authoritatively on this issue. He was a professor of physiology at the Anderson College of Medicine in Glasgow, Scotland, the head of the department of Metabolic Diseases at a leading Glasgow hospital, vice-president of the British Association of Diabetes, and a founding member of the International Diabetic Federation.

In an article for a 1971 issue of the *Journal of the History of Medicine and Allied Sciences*, “Paulescu and the Isolation of Insulin,” Murray wrote:

“Insufficient recognition has been given to Paulescu, the distinguished Romanian scientist, who at the time when the Toronto team were commencing their research had already succeeded in extracting the antidiabetic hormone of the pancreas and proving its efficacy in reducing the hyperglycaemia in diabetic dogs.

“Banting and Best are commonly believed to have been the first to have succeeded in isolating insulin. They have been hailed as its 'discoverers.' Their work, however, may more accurately be construed as confirmation of Paulescu’s findings.

“When all the circumstances are reviewed, it does appear ironical that Paulescu with all his experience might be in danger of oblivion, while the young and inexperienced Banting is remembered as if he alone had been responsible for insulin.”

The Nobel Committee may never correct its 1923 error. But the truth about the discovery of insulin cannot be suppressed for all time. Justice and honor mandate the recognition, however belated, of a forgotten medical pioneer, Nicolae Paulescu, the discoverer of insulin.

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